

- (1) an extracellular ligand association domain;
- (2) a spacer domain;
- (3) a transmembrane domain; and
- (4) one or more intracellular domains; provided that at least two of said domains in one chain are not naturally fused to each other, and wherein the spacer and/or transmembrane domains are selected to remain unassociated except in the presence of bound ligand.

20. A chimeric receptor according to Claim 19 wherein each extracellular ligand association domain is an antibody variable region ( $V_H$  or  $V_L$ ) domain, a T-cell receptor variable region domain (TCR $\alpha$ , TCR $\beta$ , TCR $\gamma$ , TCR $\delta$ ), CD8 $\alpha$ , CD8 $\beta$ , CD11a, CD11b, CD11c, CD18, CD29, CD49a, CD49b, CD49c, CD49d, CD49e, CD49f, CD61, CD41 or CD51 chain or a fragment thereof.

21. A chimeric receptor according to Claim 20 wherein each association domain is structurally different to each other.

22. A chimeric receptor according to Claim 19 wherein the ligand association domains of the chimeric receptor are a  $V_H$  domain paired with a  $V_L$  domain, two or more TCR $\alpha$ , TCR $\beta$ , TCF $\gamma$ , and/or TCR $\delta$  domains, a CD8 $\alpha$  or  $\beta$  homo- or heterodimer, CD18 paired with one or more of CD11a, b, or c, CD29 paired with one or more of CD49a, b, c, d, e, or f, and CD61 paired with CD41c and/or CD51.

23. A chimeric receptor according to Claim 19 wherein each intracellular domain is a naturally occurring polypeptide signaling sequence.

24. A chimeric receptor according to Claim 23 wherein each signaling sequence is all or part of the zeta, eta or epsilon chain derived from the T-cell receptor; CD28; CD4; CD8; the  $\gamma$  chain of an Fc receptor; a signaling component from a cytokine receptor, a colony stimulating factor receptor, a tyrosine kinase and binding domains thereof; or an adhesion molecule.
25. A chimeric receptor according to Claim 19 wherein the transmembrane domain is an oligo- or polypeptide derived from all or part of the alpha, beta or zeta chain of the T-cell receptor, CD28, CD8, CD4, CD3 $\epsilon$ , CD45 and members of the tetraspan family, a cytokine receptor, or a colony stimulating factor receptor.
26. A chimeric receptor according to Claim 19 wherein each spacer domain is a polypeptide comprising 20 to 100 amino acids.
27. A chimeric receptor according to Claim 19 wherein each independent polypeptide chain has a secretion signal sequence attached to the N-terminus of the association domain of each chain.
28. A chimeric receptor according to Claim 19 wherein the chimeric receptor has two independent polypeptide chains.
29. A chimeric receptor according to Claim 28 wherein one polypeptide chain has a ligand association domain which is a V<sub>H</sub> domain or a fragment thereof, and the other has a ligand association domain which is a V<sub>L</sub> domain or a fragment thereof.
30. A chimeric receptor of Claim 19, wherein the spacer domain is modified to remain unassociated except in the presence of bound ligand.

31. A chimeric receptor of Claim 19, wherein the transmembrane domain is modified to remain unassociated except in the presence of bound ligand.
32. A chimeric receptor of Claim 19, wherein the spacer domain is a CD8 domain.
33. A chimeric receptor of Claim 32, wherein the CD8 spacer domain is a modified CD8 spacer domain.
34. A nucleic acid sequence encoding a chimeric receptor of Claim 19 or an independent polypeptide chain thereof.
35. A nucleic acid sequence according to Claim 34 in association with a carrier.
36. A nucleic acid sequence according to Claim 35 wherein the carrier is a viral vector, a liposomal vector, a cationic lipid or an antibody.
37. A nucleic acid sequence according to Claim 35 wherein the carrier is a targeted carrier.
38. A nucleic acid sequence according to Claim 34 wherein the nucleic acid sequence is on a plasmid.
39. Plasmid pHMF374 of Figure 3.
40. An effector cell containing a nucleic acid sequence or a plasmid according to Claim 34.
41. An effector cell expressing a chimeric receptor of Claim 19.